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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,139	05/20/2002	Michael Anthony Cawthorne	0380-P02773USO	6237

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,139	CAWTHORNE ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,12-35,39,44,45,47,48 and 50-57* is/are pending in the application.

4a) Of the above claim(s) *44,45 and 50-57* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,12-35,39,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Amendment of 3/6/06 has been entered. Claims 1, 4-6, 12-35, 39, 44-45, 47-48 and 50-57 are pending. Claims 1, 4-6, 12-35, 39 and 47-48 are under examination.

The amendment has entered no new matter.

The amendment has overcome previously stated issues as follows:

The objection to the specification.

The objection to claim 1, 11, 20 and 24 for informalities.

The objection to claim 12 under 37 CFR 1.75. Examiner concurs that objection to claim 11 rather than claim 12 was intended. Since claim 11 has been cancelled, the objection has been overcome.

The objection to claim 47 under 37 CFR 1.75.

The rejection of claims 1, 12, 18, 31, 33-37 and 36-38 under 35 USC 112, 2nd paragraph.

The rejection of claims 1,4-6,9,11-39 and 47-48 under 35 USC 112, 1st paragraph, regarding new matter and lack of possession of the elements of claim 1.

The rejection of claims 1,4-6,9,11-39 and 47-48 under 35 USC 112, 1st paragraph, regarding the lack of enablement of claim 1, step d).

The rejection of claim 38 under 35 USC 112, 1st paragraph, due to its cancellation.

The rejection of claims 36-38 under 35 USC 112, 1st paragraph, due to their cancellation.

The rejection of claims 36-38 under 35 USC 101, due to their cancellation.

The rejection of claim 47 under 35 USC 112, 1st paragraph.

Claims 15, 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 15 "the diet fed to the offspring" lacks antecedent basis because base claim 14 has only referred to a diet fed to the pregnant animals.

In claim 19 "the differential levels of islet cell or B-cell mass or function" lacks antecedent basis in claim 4. It is further unclear how such "differential levels of...mass or function" can be "induced" by "comparing pregnant or non-pregnant animals", since inducing any physiological state requires a physical/chemical treatment, rather than a comparison.

Claims 1, 13,22-26, 33-34, 39 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al.

The instant claims are drawn to a method of screening for an agent having efficacy in treating an islet or B-cell dysfunction (e.g. insulin resistance) comprising providing a first biological sample obtained from a subject having such dysfunction (e.g. an insulin resistant subject), a second biological sample obtained from a normal subject, a third biological sample obtained from a subject having such dysfunction (e.g. an insulin resistant subject) who has been treated with a known treatment or compound which an islet or B-cell dysfunction (e.g. insulin sensitivity), and a fourth biological sample obtained from a normal subject who has been treated with the known treatment or compound. The method further comprises identifying at least one differentially expressed protein which is differentially expressed in said first and second biological samples, differentially expressed in said first and third biological samples, but not differentially expressed in said second or fourth biological samples. The method further comprises providing a fifth biological sample from a subject having such dysfunction (e.g. an insulin resistant subject) wherein said sample or subject has been treated with an agent, and

determining the expression Level of said at least one differentially expressed protein in said fifth sample, wherein agents which alter the expression of the Level towards that observed in the second or third biological sample have efficacy for the treatment of such dysfunction (e.g. insulin resistance).

Wang et al. sets forth that thiazolidinediones enhance insulin action and lower blood glucose in obese, insulin-resistant animals and patients with glucose intolerance or non-insulin-dependent diabetes (see Wang et al., page 1045, col. 1, Lines 1-10). Wang et al. further identifies That that troglitazone and the potent novel thiazolidinedione BRL 49653 (rosiglitazone) improves glucose tolerance, lowers hyperinulinaemia and up-regulates insulin receptors in peripheral tissues (see Wang et al., page 1045, col. 1, Line 11 through page 1406, col. 1, Line 13). To this end, Wang et al. sets forth a study that characterizes the effects of BRL 49653 on insulin resistance in Zucker and Wistar rats; such is encompassed by the claimed method for screening for an agent having efficacy in treating insulin resistance. Expression Levels of insulin were determined from several biological samples taken from both control (a normal subject, sample 2) and BRL 49653 treated (a normal subject treated with a compound that alters insulin sensitivity, sample 4) lean Zucker rats as well as control (an insulin resistant subject, sample 1) and BRL 49653 treated (an insulin resistant subject treated with a compound that alters insulin sensitivity, sample 3) fatty Zucker rats, which is encompassed by the claimed steps of providing a first through fourth biological sample (see Wang et al., Tables 1 and 2 and page 1406, col. 1, Lines 14 through col. 2, Line 22). Wang et al. further characterizes the differential expression insulin in the above identified rats wherein control Lean Zucker rats (sample 2)

expressed at 32.0 +/- 8.4., 7-day BRL 49653 treated Lean Zucker rats (sample 4) expressed at 28.2, +/- 4.3,. control fatty Zucker rats (sample 1) expressed at 397.4, +/- 26.8*, and 7-day BRL 49653 treated fatty Zucker rats (sample 3) expressed at 279.1, +/- 20.8 (see Wang et al., Tables 1 and 2). As such, insulin was identified as being differentially expressed between the first and second samples (397.4, +/- 26.8 vs. 32.0, +/- 8.4), differentially expressed between the first and third samples (397.4, +/- 26.8 vs. 297.1 , +/- 20.8), but not differentially expressed between the second and forth samples (32.0, +/- 8.4 vs. 28.2, +/- 4.3), such is encompassed by the step of identifying at least one differentially expressed protein. In the instant case, the treatment of fatty Zucker rats with BRL 49653 is encompassed by the claimed step of providing a fifth biological sample from a subject that has been treated with an agent, as the instant claims do not exclude the embodiment wherein the screened agent may also be the compound that alters insulin sensitivity. As such, the BRL 49653 compound acts as an agent which alters the expression level of insulin to that observed in the above identified third biological sample. Wang et al. sets forth that the results of the study demonstrates a previous observation that thiazolidinediones, specifically by the administration of effective amount of BRL 49653, have an impact on insulin resistant subjects (see Wang et al., page 1407, col. 1, Line 34 through col. 2, Line 4). Claim 1 is thus anticipated.

The limits of instant claim 13 are inherent to fa/fa rats; see instant spec pg 28 for evidence. Note claim 13 merely refers to the nature of the dysfunction and does not positively require that there be any dietary treatment conducted.

The limits of instant claim 22 are inherent to fa/fa rats; see instant spec page 2, lines 113-20 for evidence. Limits of further dependent claims 23-26 are shown by the reference (pg 1405).

Regarding instant claims 33-34, Wang et al. sets forth the isolation and measurement of insulin in the disclosed methodology as well as the characterization the role of insulin and BRL 49653 in the insulin action on both Wistar and Zucker rats (see Wang et al., page 1405, col. 1, Lines 1-25 and page 1406, col. 1 , Line 50 through col. 2, Line 22).

Regarding instant claim 39, Wang et al. sets forth the preparation of daily BRL 49653 dosages in a 10% sucrose solution and orally administering to Zucker rats relied upon in the study (see Wang et al., page 1406, col. 1 , 29-48).

Regarding instant claim 47, Wang et al measure the insulin in body fluid (plasma) samples.

Claims 1,4,6,20-26,32-34,36,39 and 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Larsen et al in view of Wang et al.

Larsen et al have been previously cited for teaching one to identify/screen for agents that alter the expression levels of proteins that have been identified as being differentially expressed in diabetic vs. non- diabetic subjects. Larsen et al consider "diabetes" as encompassing numerous diabetes related diseases, including insulin resistance (page 10). Applicant has urged that Larsen et al do not show the comparison of the instantly four recited subjects but, rather show use of only two of the recited subjects, in the process of identifying differentially expressed proteins. As noted supra, however, Wang et al show a method involving the use of a compound that has a known effect on an islet/B-cell dysfunction (insulin resistance) in experiments that use four

groups of rats that correspond to the instantly recited subjects; Wang et al show the identification of a protein (insulin) whose expression is altered by the treatment in the group of rats having the dysfunction. In order to more fully control for the effects of altered protein expression, by comparing the effects of a compound that has a known effect upon an islet/B-cell dysfunction upon both subjects with the disorder and subjects without the disorder, it would have been obvious to have identified differentially expressed proteins by using four groups of subjects, in the manner of Wang et al; once the differentially expressed proteins had been identified it would have been obvious to further determine the effect of a test compound/test agent upon a 5^{th} group of subjects having the disorder and, for further control, to compare results obtained with the fifth group of subjects against the subjects having the dysfunction but which were treated with no test compound/test agent. Thus claim 1 would have been obvious. Dependent claims 4, 6, 20-21, 32-34, 39 and 48 are rejected for reasons of record over the disclosure of Larsen et al.

Instantly claims 22-26 are added to the rejection, because of the disclosure of Wang et al concerning use of BRL 49653.

Instantly dependent claim 47 is added to the rejection because the claim now encompasses a larger Markush group of samples.

Claims 1 4-5, 12, 20-23, 26 32-34 and 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edvardsson et al in view of Wang et al.

Edvardsson et al have been noted previously for teaching how to identify proteins that are differentially expressed in the liver of ob/ob mice in response to the agonist WY 14,643. Applicant has urged that Edvardsson et al do not show the comparison of the instantly four

recited subjects. As noted supra, Wang et al show a method involving the use of a compound that has a known effect on an islet/B-cell dysfunction (insulin resistance) in experiments that use four groups of rats that correspond to the instantly recited subjects; Wang et al show the identification of a protein (insulin) whose expression is altered by the treatment in the group of rats having the dysfunction. As set forth supra concerning the combination of Larsen et al in view of Wang et al, it would have been obvious to identify the differentially expressed proteins with the use of the four subjects instantly recited, and to then further determine the effect of a test compound/test agent upon a 5th group of subjects having the disorder and, for further control, to compare results obtained with the fifth group of subjects against the subjects having the dysfunction but which were treated with no test compound/test agent. Thus claim 1 would have been obvious.

Instant dependent claims 4-5, 12, 20-23, 26, 32-34 and 48 are rejected as previously over Edvardsson et al.

Instantly dependent claim 47 is added to the rejection because the claim now encompasses a larger Markush group of samples.

Claims 1, 4-6, 12-35, 39 and 47-48 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 14-25, 27-28 and 30-33 of copending Application No. 09/980,422. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claim 1 and copending claim 1 have been amended in a parallel manner. The examiner considers that there would yet be common embodiment encompassed by the two sets of claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's amendment necessitated the new ground(s) of rejection over the prior art presented in this Office action (any new grounds not thus necessitated relate to mere 112, second para. informalities). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 5/30/06 DAS

David A Saunders

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ART UNIT 182 / 1644